

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF
PATENT APPEALS AND INTERFERENCES

Application of

Applicants : Catherine M. Verfaillie and Yuehua Jiang
Application No. : 10/561,826
Filed : October 17, 2006
Title : Neuronal Differentiation of Stem Cells
Examiner : Chang Yu Wang
Attorney Docket No. : 890003-2006.1
Art Unit : 1649

Cleveland OH 44114

Date: October 17, 2011

MAIL STOP APPEAL BRIEF- PATENTS
Commissioner for Patents
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APPELLANTS' REPLY TO EXAMINER'S ANSWER

Sir:

Appellants file this Reply Brief to address statements made by the Examiner in the Examiner's Answer.

Appellants do not agree with these statements and request that they be allowed to clarify their position in this Reply.

(1)

On page 15 of the Examiner's Answer, the Examiner makes the following statement:

Appellants acknowledge that it is obvious to sequentially add growth factors because at the end the culture medium would inherently encompass added growth factors.

The Examiner does not cite specific text in the Appeal Brief or in any of Appellants' responses at which this "acknowledgement" was made.

Appellants have found their statements on the issue. Their position is extremely qualified.

Appellants' Statements in Response to the Examiner's Statements in Final Office Action dated December 24, 2008

The Examiner's rationale (in the final Office Action) appeared to be the following: "Although the instant method recites adding bFGF, FGF8, SHH, BDNF [sic] sequentially, *at the end of the final steps, the culture medium contains the identical growth factors as those in Studer's* to induce neuronal differentiation." Page 7 of the Office Action. Italics added. Appellants response (on page 6) was as follows:

Applicants assume, for argument's sake (although this has not been tested), that adding the factors to the nestin-positive cells sequentially would produce the same result as simultaneous exposure if one were to add them all *within minutes, or perhaps even hours, of each other*. But where each individual step is carried out for *at least seven days*, one would not have expected the same result as simultaneous exposure. One would not have known what to expect. Accordingly, Applicants seek to incorporate the limitations of previous claim 4, indicating that each step is carried out for at least seven days.

Each factor induces a specific phenotypic effect. If the factors are all added simultaneously, it is not reasonably predictable that the phenotype will be the same as the phenotype produced by exposing the cell to the factors sequentially for an extended period. Accordingly, performing the method sequentially, with sufficient time between each step, would not have reasonably predicted cells with the same phenotype. More likely than not, the cells should be different.

Appellants also addressed this issue in their Appeal Brief on pg. 12. Appellants understood the Examiner's point to be the following: Sequential addition would inherently encompass adding the factors within a matter of seconds or minutes or even hours (i.e., before they have a chance to affect the cells and alter the phenotype). It would have been obvious to add all the factors one at a time at the beginning of the procedure.

Appellants could see the Examiner's logic as it pertained to claims 1 and 13, which did not recite the time period of seven days for each step. Accordingly, Appellants incorporated (into claims 1 and 13) the limitations of claim 4, that each step is at least seven days.

Accordingly, Appellants merely acknowledged that the end result might be the same when factors are added all together or very close in time (e.g., seconds or minutes) such that none of the factors has sufficient time to act alone.

(2)

On page 15 of the Examiner's Answer, the Examiner makes the following statement:

However the appeal claims have been amended which are different from original claims. Appellants cannot use the instant claims to argue against the responses from different Office Actions because these different Office Actions were used to address different claim limitations in different claim amendment [sic].

In point of fact, current claim 1 incorporates the limitations of original claim 4, which has been rejected from the outset for the same reasons that the Examiner presented in the first non-final Office Action.

Original claim 1 did not recite the limitation of performing each step for seven days. Appellants incorporated the limitations of original claim 4 into original claim 1. So, from the outset, the Examiner rejected original claim 4 (i.e., *de facto*, current claim 1).

(3)

On page 20 of the Examiner's Answer, the Examiner makes the following statements:

In response, although the instant method recites adding bFGF, FGF8, SHH and BDNF sequentially, the claimed method is only directed to inducing neuronal differentiation and is not directed to differentiation into specifically defined proportions of specific types of neurons. Note that the claimed method and the cited references are directed to the same goal (neuronal differentiation from stem cells) using the same materials (bFGF, FGF8, SHH and BDNF). The claimed method is directed to inducing neuronal differentiation using the same growth factors (bFGF, FGF8, SHH and BDNF) and the same ES cells and similar culture duration, which are taught by the cited references. Although the claimed method alters the way of adding growth factors in the methods of Studer and Lee, and phenotypical cell types may have different proportions during the recited culturing

procedures, at the end of the steps, the result of neuronal differentiation from stem cells including dopaminergic, serotonergic and GABAergic neurons is expected as taught by Studer and Lee (see p. 9, [0125], p. 9 [0128]; p. 14, example 5, in particular).

Accordingly, the Examiner appears to take the position that the Studer and/or Lee discrete differentiation protocols (i.e., for each of GABA-ergic, dopaminergic, and serotonergic neurons, oligodendrocytes, and astrocytes) and the five stages are irrelevant because the claims are not directed to a specific neuronal end product. Thus, the Examiner seems to be taking the position that it would have been obvious to mix and match factors and sequences from the different discrete protocols of Studer and/or Lee. Appellants disagree for the following reasons.

The discrete protocols of Studer and Lee are indeed relevant because each protocol is specifically designed to produce a desired end product. Neither Studer nor Lee suggest taking pieces from one discrete protocol and mixing them together with pieces from a different discrete protocol to generate a mixture of end products, as the Examiner seems to suggest. Furthermore, it is not suggested by either reference that, if one were to do that, any functional end product would even be obtained.

Accordingly, the discrete protocols in the cited art are relevant to the issue of obviousness even though Appellants' claims are not directed to a particular end product. The claimed protocol does not correspond to any of these discrete protocols. And there is no suggestion to modify any of them to arrive at the claimed protocol.

(4)

On page 21 of the Examiner's Answer, the Examiner applies *KSR International Co. v. Teleflex, Inc.*, 82 USPQ2d 1385(2007), the Examination Guidelines in the *Federal Register* (Vol. 72, No.195 October 10, 2007) and *Manual of Patent Examining Procedure* (Revision 6, September 2007). There are six points.

- A) Combining prior art elements according to known methods to yield predictable results.

- B) Simple substitution of one known element for another to obtain predictable results.
- C) Use of known technique to improve similar products in the same way.
- D) Applying known technique to a known product ready for improvement to yield predictable results.
- E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success.

These first five have to do with predictability. Appellants have already commented on and provided a Declaration on this issue.

The sixth point is that there would be a motivation to lead one of ordinary skill in the art to modify the prior art references to arrive at the claimed invention (emphasis by Appellants).

- F) Some teachings, suggestion, or motivation in the prior art that would lead to one of ordinary skill to modify the prior art reference to arrive at the claimed invention.

As Appellants have explained in their responses and Appeal Brief, even combining the references one would not, in fact, arrive at the claimed invention (i.e., produce a method having all of the limitations of the Appellants' claims).

Appellants do not believe that any fees are due with this filing. In the event that fees are incurred, however, the Commissioner is hereby authorized to charge any additional fees required to our Deposit Account 20-0090. Appellants hereby authorize the Commissioner under 37 C.F.R. §1.136(a)(3) to treat any paper that is filed in this application which requires an extension of time as incorporating a request for such an extension.

Respectfully submitted,



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